ABSTRACT

Neonatal ACTH Alters Hypothalamic-Pituitary-Adrenal and -Gonadal Function; Correlation with Developmental Changes in Forebrain Monoamine Innervation. Stephen E. Alves,[1] Homayoon M. Akbari,[2] George M. Anderson,[2] Efrain C. Azmitia[1] and Fleur L. Strand[1]. [1]Department of Biology, New York University, Washington Square, New York, NY, and [2]The Yale Child Study Center, Yale University School of Medicine, New Haven, CT

The effects of adrenocorticotropin (ACTH) administration on the developing female rat brain were investigated. Female Sprague-Dawley rat pups were injected with either ACTH 1-24 (0.5mg/kg) or saline vehicle once daily, from postnatal day 1 (day of birth) to day 7. Forebrain monoamine (MA) innervation, pituitary-adrenal response and reproductive parameters were examined at several ages. ACTH administration, which greatly elevated plasma corticosterone (CORT) levels, exerted an acute stimulatory effect on the maturation of the forebrain MA systems, and produced long-term changes in these systems in the adult brain. Adrenocortical stimulation resulted in an hypertrophy of the neonatal adrenal glands and significantly elevated peak basal CORT levels through to pubescence. These alterations were correlated with a disruption in the HPG system, manifested by a delay in reproductive maturation, decreased female sexual behavior at young adulthood, and significantly decreased plasma estradiol levels during proestrus. Neonatal ACTH also appears to have altered adult HPA reactivity to stress, as measured by significantly altered stress hormones following a stressor. These findings demonstrate that the developing female rat brain is highly susceptible to elevated pituitary/adrenal stress hormone exposure during the neonatal period. Elevated ACTH/CORT levels early in postnatal life appear to act directly on the MA systems, increasing fiber outgrowth and the synthesis of these neurotransmitters. Consequently, as the MAs, in turn, act as differentiation/regulatory factors in the developing CNS, stimulated growth of the MA systems will further affect the proliferation/maturation of other neural systems. This disruption in neurocircuitry, together with a lingering adrenocortical hypersecretion early in life, is probably responsible for the observed alterations in the functioning of two important neuroendocrine regulatory systems in the female rat, the HPA and the HPG axes.